SUMMARY OF SAFETY AND EFFECTIVENESS

I. GENERAL INFORMATION

DEVICE GENERIC NAME:	Intervertebral Body Fusion Device
DEVICE TRADE NAME:	Ray Threaded Fusion Cage (TFC)™
APPLICANT'S NAME:	Surgical Dynamics, Inc. division of United States Surgical Corporation 111 Glover Avenue Norwalk, CT 06856
PREMARKET APPROVAL (PMA) APPLICATION NUMBER:	P950019
DATE OF PANEL RECOMMENDATION:	May 23, 1996
DATE OF NOTICE OF APPROVAL TO THE APPLICANT:	

II. INDICATIONS FOR USE

The Ray TFC™ is indicated for use with autogenous bone graft in patients with degenerative disc disease (DDD) at one or two levels from L2 to S1. These DDD patients may also have up to Grade I spondylolisthesis at the involved level(s). The Ray TFC™ is to be implanted via an open posterior approach.

DDD is defined as back pain of discogenic origin with degeneration of the disc confirmed by history and radiographic studies. These patients should be skeletally mature and have had six months of non-operative therapy.

III. DEVICE DESCRIPTION

The Ray TFC™ is a hollow, threaded cylinder available in eight sizes. The sizes (diameter x length) are: 12mm x 21mm; 12mm x 26mm; 14mm x 21mm; 14mm x 26mm; 16mm x 21mm; 16mm x 26mm; 18mm x 21mm; and 18mm x 26mm. Each device has external 60° threads with flat crests and roots to allow for primary fixation into a pre-tapped intervertebral cavity. The device has multiple small transverse holes to enhance bony ingrowth. The Ray TFC™ is used with anterior and posterior end caps which are available in corresponding diameters of 12mm, 14mm, 16mm, and 18mm.

The Ray TFC™ is manufactured from titanium 6Al-4V (extra low interstitial) alloy which conforms to American Society Testing and Materials (ASTM) F136-92. The anterior and posterior end caps are manufactured from ultra-high molecular weight polyethylene

(UHMWPe) which conforms to ASTM F648-84. The Ray TFC™ and end caps are provided sterile.

The Ray TFC™ and end caps are implanted using a defined set of instruments which are available in two categories: size specific and universal. The size specific instruments, which correspond to the diameter of the Ray TFC™, include the following: tang retractor; vertebral drill; vertebral tap; and cage insertion instrument. The universal instruments, which are used regardless of the diameter of the Ray TFC™, include the following: T-handle, end cap insertion instrument, end cap removal instrument; bone packing instrument; impactor cap (tang retractor cap); small/large ganglion retractors; and chisel. All instruments are manufactured from stainless steel which conforms to ASTM F899-94. All instruments are provided nonsterile and must be sterilized prior to use or reuse.

IV. CONTRAINDICATIONS

The Ray TFC™ should not be implanted in patients with an active infection at the operative site.

V. WARNINGS

Implantation of a single cage per involved level is not recommended. The implantation of a single cage has been associated with cage fracture.

VI. PRECAUTIONS

Prior to use, the physician should be trained in the surgical procedure recommended for the use of this device.

Safety and effectiveness have not been established for patients with the following conditions: previous fusion attempt at the involved level(s); spondylolisthesis greater than Grade I; three or more levels to be fused; concomitant conditions requiring steroids; systemic or terminal illness; active drug abuse; pregnancy; gross obesity; or significant loss of quantity or quality of vertebral bone stock usually due to osteoporosis.

The Ray TFC™ and end caps are packaged sterile. Do not use if outer package is opened or damaged. Single use only. Do not re-use. Do not resterilize.

Avoid exposure to freezing temperatures, as this could adversely affect the polyethylene end caps.

Instruments for implantation of the Ray TFC™ and end caps are provided non-sterile and must be sterilized prior to use.

VII. ALTERNATIVE PRACTICES AND PROCEDURES

Nonoperative alternative treatments may include, but are not limited to, physical therapy, medications, braces, chiropractic care, or exercise programs. In addition, there are alternative spinal fusion techniques. These include, but are not limited to, posterior lumbar interbody fusion (PLIF) procedures without instrumentation, anterior lumbar interbody fusion (ALIF) procedures without instrumentation, combined anterior and posterolateral (360°) fusion procedures, anterior/anterolateral spinal systems (e.g., plate and screw systems), or posterior spinal systems (e.g., hook and rod systems).

VIII. POTENTIAL ADVERSE EFFECTS

From the investigational device exemption (IDE) G910006, a total of 236 patients were evaluated for adverse events with the Ray TFC™. The adverse events (complications) were stratified into operative and postoperative categories.

The operative complications are presented in Table 1. The rates represent the incidence rates (i.e., number of occurrences of a particular complication divided by the total number of patients enrolled in the study).

Table 1 - Operative Complications

Complication	Rate
dural tear	9.3% (22/236)
instrument malfunctions[1]	5.1% (12/236)
improper device placement	4.2% (10/236)
hemorrhage	2.1% (5/236)
neural structure injury	0.8% (2/236)
incorrect level	0.4% (1/236)

[1]The instruments have since been redesigned with the intent to simplify their use and to address the reported malfunctions.

The postoperative complications are presented in Table 2. Wound infections, urinary retentions, cerebral spinal fluid (CSF) leakages, soft tissue hematomas, premature ejaculation, malposition, and pneumothorax occurred in the early postoperative time frame and were transient. One patient died of causes unrelated to the device or procedure late in the study.

Table 2 - Postoperative Complications

Complication	Rate
pain, *unresolved pain at 24 months*	11.0% (26/236) *3.0% (7/236)*
neurological deficit *unresolved deficit at 24 months*	4.7% (11/236) *2.5% (6/236)*
surgical interventions[1]	3.4% (8/236)
wound infection	2.5% (6/236)
soft tissue hematoma	1.3% (3/236)
CSF leakage	1.3% (3/236)
urinary retention	0.8% (2/236)
ileus	0.4% (1/236)
device breakage	0.4% (1/236)
epidural fibrosis	0.4% (1/236)
premature ejaculation	0.4% (1/236)
pneumothorax	0.4% (1/236)
death (unrelated to device/procedure)	0.4% (1/236)

[1]includes 3 revisions, 1 removal, 0 reoperations, and 4 supplemental fixations (see definitions below)

A revision is a procedure which adjusts or in any way modifies the original implant configuration (e.g., adjusting position of original configuration, removal with replacement of component). A removal is a procedure which removes one or more components of the original implant configuration without replacement of any components. A reoperation is a procedure which involves any surgical procedure at the involved level(s) which does not remove, modify, or add any components. A supplemental fixation is a procedure in which additional instrumentation not approved as part of the protocol is placed. This may include supplemental placement of a rod/screw system or a plate/screw system.

Patients who had surgical interventions in this study have already been accounted for in the other complications identified in Tables 1 and 2 above. The complications that led to these surgical interventions include the following. Three patients underwent revisions: 1) urinary problems led to one device being removed and reimplanted hours postoperatively; 2) too small of a device led to it being removed and replaced with a larger device the same day as the original surgery; and 3) improper device placement led

to the device being repositioned 40 days postoperatively. One patient underwent a device removal three years postoperatively due to neurological deficit and pain. Four patients underwent supplemental fixations to have pedicle screw systems added at 240, 329, 362, and 827 days postoperatively, respectively.

IX. MARKETING HISTORY

The Ray TFC™ has been marketed in approximately 16 international countries. It has not been withdrawn from marketing for any reason relating to its safety or effectiveness.

X. SUMMARY OF PRECLINICAL STUDIES

Nonclinical tests were conducted to characterize the mechanical properties of the Ray TFC™.

A. Static Superior-Inferior Compression Testing

The first set of static compression tests of the Ray TFC™ was performed using wood blocks as the vertebral model. Although yield strength (load) is typically defined as stress (load) corresponding to 0.2% of permanent deformation, it was defined as 0.001 inches of permanent deformation, a more conservative estimate of yield strength, in this set of static tests. Five samples of each cage were tested. Except for the 14mm cage, which had one outlier that was not included in the average results, all data are included in the average. The average static yield strengths were:

Ray TFC™ Size	Static Yield Strength
14mm x 21mm	2167 ± 142 N (487 ± 32 lbs)
16mm x 21mm	2114 ± 138 N (475 ± 31 lbs)
16mm x 26mm	2203 ± 93 N (495 ± 21 lbs)
18mm x 26mm	2826 ± 312 N (635 ± 70 lbs)

A second set of static compression tests was performed using steel blocks as the vertebral model because of the amount of deformation that the oak blocks underwent during compression. Additionally, the static yield load was redefined as 0.2% of permanent deformation. Five samples of each cage were tested. The average static yield strengths were:

Ray TFC™ Size	Static Yield Strength
12mm x 26mm	13617 ± 2648 N (3060 ± 595 lbs)

16mm x 26mm	10458 ± 1847 N (2350 ± 415 lbs)

The device's compressive strength greatly exceeds the compressive strength of bone which is estimated to be approximately 1500 N (337 lbs).

B. **Fatigue Testing**

Fatigue testing was performed on the Ray TFC™ using oak blocks as vertebral models. All of the tests involved a single cage construct with the end caps in place. There were two sets of fatigue tests, both involved loading the device constructs at 4 Hz. In the first set of tests, the loads were applied without preloading until 10 million cycles were reached or failure (defined as a microfracture). In the second set of tests, the cages which showed microfractures prior to 5 million cycles in the first set of tests were retested past 7 million cycles. This was to show that the devices with microfractures could still be capable of carrying the applied loads.

A total of 38 samples (6-17 samples per cage diameter) were tested. This includes the four (4) cages that were retested. The 12mm, 14mm, and 16mm Ray TFC™s all had fatigue strengths (i.e., endurance limits) of approximately 1335 N (300 lbs) at cycles ranging from five (5) million to over 15 million. The 18mm Ray TFC™ had a fatigue strength of approximately 890 N (200 lbs) at cycles ranging from eight (8) million to over 15 million. Five (5) million cycles typically represents the number of loading cycles a device might experience within two years. This assumes moderate loading and the device's goal of stabilizing until fusion occurs within those two years. Because of the way the fatigue testing was performed, the endurance limits for each cage size at five (5) million cycles could not be derived. It is expected that if the device was tested in that manner, the endurance limits at five (5) million cycles would be greater than those reported above.

After testing, there were a total of eight (8) of 38 cages with microfractures, but all of the cages stayed intact and were capable of withstanding the applied loading. There were no reported end cap dislodgments. Although the Ray TFC™ can be expected to withstand anticipated physiologic fatigue loads, the Ray TFC™ should be implanted as a pair based on the resulting fatigue strengths. This is reflected in the Warnings section of the labeling.

C. **Static Closure (End Cap) Testing**

Static loads were applied to the anterior and posterior end caps to determine the loads required to insert or extract the end caps from the Ray TFC™. Five samples were tested for each Ray TFC™ and end cap construct. The average insertion and extraction loads were:

End Cap	Insertion Force	Extraction Force
14mm (posterior)	55 N (12 lbs)	58 N (13 lbs)
16mm (posterior)	68 N (15 lbs)	97 N (22 lbs)
18mm (posterior)	65 N (15 lbs)	112 N (25 lbs)
14mm (anterior)	not tested	85 N (19 lbs)
16mm (anterior)	not tested	212 N (48 lbs)
18mm (anterior)	not tested	138 N (31 lbs)

Based on the expected minimal loading on the end caps, the end caps should not become dislodged from the Ray TFC™.

D. **Expulsion Testing**

The loads required to dislodge a Ray TFC™ when implanted between two calf vertebrae were measured. Two calf vertebrae and the adjacent disc were potted in cement. Pull-out forces up to 500 lbs or until a displacement of 0.01 inch were applied to the device. Five samples of each were tested. The average pull-out strengths were:

Ray TFC™ Size	Pull-Out Strength
14mm x 21mm	2225 N (500 lbs) - no failure
16mm x 21mm	2198 N (494 lbs)
18mm x 26mm	2092 N (470 lbs)

Loading of this type and magnitude are not expected in the spine where the Ray TFC™ is to be placed. Therefore, expulsion of the Ray TFC™ is not expected with proper sizing and placement.

XI. SUMMARY OF CLINICAL INVESTIGATIONS

A clinical study of the Ray TFC™ was conducted in accordance with an approved IDE G910006.

A. **Objective**

The objective of the study was to determine the safety and effectiveness of the Ray TFC™ in stabilizing and fusing the diseased level(s) when compared to literature controls.

B. Inclusion and Exclusion Criteria

The inclusion criteria were males and females at least 18 years of age with symptomatic DDD at 1 or 2 levels from L2 to S1. Symptomatic DDD was defined as one or more of the following conditions: low back pain with or without sciatica; pain reproduction during provocative discography; annular degeneration; disc herniation; loss of disc height; and/or osteophytes. The inclusion criteria involved primary and secondary surgery but no previous PLIF at the involved level(s). Note that based on Panel input, the definition for DDD was refined to that reflected in Section II above, Indications for Use.

The exclusion criteria were as follows: anatomic anomalies of the bone to be fused; previous fusion at the same level; spondylolisthesis greater than Grade I; need for three or more levels fused; concomitant conditions requiring steroids; systemic or terminal illness; active drug abuse; significant endplate sclerosis at the diseased level; active infection; DDD of the cervical or thoracic regions; and pregnancy.

All patients were implanted via a posterior surgical approach. Autogenous bone graft was packed into the Ray TFC™ devices after implantation.

C. Patient Population and Demographics

The Ray TFC™ study is comprised of 62% (147/236) males and 38% (89/236) females. The mean age at time of study enrollment was 41.4 years with a range of 19 to 80 years. 40% (95/236) of the patients were on worker's compensation. 7% (17/236) were involved in ongoing litigation. 27% (63/236) were smokers and 45% (106/236) had prior back surgery.

All 236 patients enrolled in the Ray TFC™ study had a diagnosis of DDD. These patients presented at least one or more of the following preoperative DDD diagnostic criteria: 98% (232/236) low back pain; 39% (92/236) pain reproduction upon discography; 66% (155/236) herniated disc; 59% (139/236) degenerated annulus; 44% (104/236) disrupted annulus; 47% (112/236) disc height loss; and 17% (39/236) osteophytes.

A total of 298 levels were implanted in 236 patients. The distribution of the levels were: 0% at L2-L3; 6% (17/298) at L3-L4; 43% (128/298) at L4-L5; 1% (3/298) at L5-L6; and 50% (150/298) at L5-S1. Of the 236 patients, 74% (175/236) had one-level fusions, 25% (60/236) had two-level fusions, and <1% (1/236) had three-level fusions. There were 10 single cages and 288 pairs of cages implanted for a total of 586 cages implanted.

D. Evaluation Schedule

Patients were evaluated preoperatively, immediately postoperatively (i.e., at hospital discharge), at 6 weeks, 3 months, 6 months, 12 months, 18 months (optional), 24 months, and biennially thereafter until the last patient had his/her two-year evaluation. Radiographic studies were conducted at 6 months, 12 months, and 24 months

postoperatively. Optional films were taken at 18 months.

E. Patient Accountability

A total of 236 patients were enrolled at 10 investigational sites in the United States by 13 investigators. As of March, 1996, all patients but the one unrelated death had reached his/her two-year postoperative time point. Follow-up evaluations, which included an assessment of fusion, pain, function, and muscle strength, were performed on 209 of 235 patients (89%) at the two-year time point. Complete follow-up evaluations (i.e., measurement of each of the four major outcome parameters) were performed on 199 of these 209 patients (95%).

F. Study Design and Analyses

1. Literature Study Control

Literature controls were employed in this study. Outcomes of patients implanted with Ray TFC™s were compared to outcomes of patients who received PLIFs. Literature references were deemed acceptable as controls if the patients were considered to have DDD; this group may or may not have had spondylolisthesis of Grade I or less. This differs from the Ray TFC™ group in which all patients had back pain due to DDD and had no greater than Grade I spondylolisthesis.

The literature controls used in this study had many differences relative to the Ray TFC™ population with respect to the indication for use, the method by which DDD was defined, the number of levels fused, the age of the patients, the types of outcome criteria assessed, the method of outcome assessment, the definitions for successful outcome, the duration and nature of follow-up, the incidence of previous back surgery at the same level, and whether the patients were affected by more than two psychological/behavioral risk factors (e.g., alcoholism, drug abuse).

Use of a literature control group was common at the time of the submission of this study, although it is now recognized as less desirable than a randomized, concurrent control study. The advantages of using a randomized, concurrent control reflects the disadvantages of literature controls. In general, in a randomized, concurrent control study, potential bias is eliminated or at least reduced, unknown or known baseline factors tend to be balanced between the two groups, the statistical properties of hypothetical tests are improved, time trends are controlled because of concurrency, and the results tend to be more successfully convincing.

2. Retrospective Study Control

In addition to using literature controls, the use of a retrospective control group was proposed. This proposed additional control group consisted of retrospective data

from 187 patients who had PLIFs without instrumentation for the treatment of DDD. The data were taken from five of the investigators involved in the original IDE study. 51% (95/187) of the patients had reached the one-year postoperative time point and 19% (36/187) had reached the two-year postoperative time point. As with the literature control, the patient population of the retrospective control group had many differences relative to the Ray TFC™ population. The retrospective control data were not used in comparing safety and effectiveness information based on the major differences between the two patient populations that could lead to invalid conclusions. Some of the main reasons for not considering this retrospective control group were that 82% of the retrospective group received allograft instead of autograft material, only 19% of the patients have two years of postoperative data, there was a retrospective determination of the Prolo Scale (i.e., pain and function scores), the subjective nature of the fusion assessments, and the patient selection bias.

3. Data Pooling

There were two device configurations involved in the IDE study, a hydroxylapatite (HA) coated Ray TFC™ and a non-HA coated Ray TFC™. The HA coating had no statistically different effect on the subject patient population through longitudinal analyses (using Generalized Estimating Equation (GEE) model). Therefore, the HA and non-HA data were pooled. As reflected in Section III above, Device Description, only the non-HA coated Ray TFC™ is to be marketed.

Pooling the data between investigational sites was justified based on statistical analyses using the chi-squared test. Pooling the data between binary stratified groups (e.g., 1-level versus 2-levels, smokers versus nonsmokers) was also justified based on longitudinal analyses using GEE models.

G. **Effectiveness Analyses**

The effectiveness variables included an assessment of fusion at the involved level(s), pain, function, and muscle strength. In some cases, only partial data were available (i.e., not all of the four outcome measures were obtained for all patients at all follow-up points). In these cases, all available outcomes for fusion, pain, function, and muscle strength were summarized in these analyses. Therefore, the number of patients included in the assessment of the four major outcomes varies slightly due to missing data. Because all of the patients had reached his/her two-year postoperative time point, the effectiveness analyses involved the 24 month time point.

H. **Effectiveness Analysis - Fusion**

Successful fusion was defined as no motion on a flexion/extension series of x-rays at the involved level(s), no halo around the implant, no bone sclerosis around the implant, and increased or maintained bony density within the implant. All four of the criteria had to

be met for successful fusion. In cases where two levels were implanted, both levels must have been fused in order for that patient to be considered fused. Both the IDE investigator and an independent radiologist reviewed the films. The independent radiologist reported fusion in all of the films that were available for review. A "nonfusion" determination by an investigator outweighed a "fusion" determination by the independent radiologist. The successful fusion rate at 24 months was 92% (183/200).

I. **Effectiveness Analysis - Pain**

Pain was measured on the Prolo Scale. The "functional" grade of the Prolo Scale ranks the pain responses and effect of pain on activities of daily living. This portion of the Prolo Scale is a 5-point scale where F1 = total incapacitation, F2 = mild to moderate level of low back pain and/or sciatica, F3 = low level of pain but able to perform all activities except sports (use of occasional prescription analgesics), F4 = no pain but has one or more recurrences of low back pain or sciatic (occasional over-the-counter analgesics), and F5 = complete recovery and able to perform all previous sports activities.

The distribution of pain scores preoperatively and at 24 months is shown in Table 3 below.

Table 3 - Distribution of Pain Scores

Pain Level	Preoperative Rate	24 Month Rate
F5 (best)	0%	29% (61/209)
F4	1% (3/236)	26% (54/209)
F3	8% (18/236)	22% (45/209)
F2	88% (208/236)	23% (49/209)
F1 (worst)	3% (7/236)	0%

All patients experiencing an improvement by at least one level in the pain score relative to their preoperative score were considered to have a successful result in terms of the pain outcome measure. The successful pain rate at 24 months was 76% (158/209).

It is important to distinguish between patients with a successful pain outcome and the amount of pain experienced by patients after implantation with the Ray TFC™. A successful outcome did not necessarily mean that a patient experienced no pain; instead, it means that there was at least one level of improvement.

J. **Effectiveness Analysis - Function**

Like the pain parameter, function was also measured on the Prolo Scale. The "economic" grade of the Prolo Scale expresses the patient's capacity for gainful employment or

alternative comparable pursuits (e.g., housework, retirement activities, etc.). This portion of the Prolo Scale is a 5-point scale where E1 = complete invalid; E2 = no gainful occupation (capable of independent locomotion and self care, but unable to hold job, perform housework, attend school, or continue retirement activities); E3 = able to work (attend school, participate in retirement activities, do housework) but not at previous occupation or level of activity); E4 = working at previous occupation on part-time or modified status (attending school, doing housework, preforming retirement activities); and E5 = able to work at previous occupation without any restrictions (attend school, do housework, perform retirement activities).

The distribution of function scores preoperatively and at 24 months is shown in Table 4 below.

Table 4 - Distribution of Function Scores

Function Level	Preoperative Rate	24 Month Rate
E5 (best)	3% (7/236)	43% (90/209)
E4	9% (21/236)	23% (48/209)
E3	26% (62/236)	18% (38/209)
E2	61% (143/236)	16% (33/209)
E1 (worst)	1% (3/236)	0%

All patients maintaining or experiencing an improvement by at least one point in the function score relative to their preoperative score were considered to have a successful result in terms of the function outcome measure. The successful function rate at 24 months was 96% (200/209).

K. **Effectiveness Analysis - Muscle Strength**

Muscle strength was evaluated bilaterally at eight sites: hip flexion, hip extension, hip abduction, hip adduction, knee flexion, knee extension, ankle plantarflexion, and ankle dorsiflexion. Each of the sites was measured on a 6-point scale ranging from 0 (no evidence of contractility) to 5 (complete motion against gravity, full resistance).

The average mean strength score was 4.94 ± 0.27 preoperatively and 4.99 ± 0.05 at 24 months. Maintenance or improvement in mean muscle strength score was required in order for the patient to be considered a success. The successful muscle strength rate at 24 months was 95% (197/208).

L. **Effectiveness Analysis - Disc Height**

In addition to the measuring the four major effectiveness variables, the anterior and

posterior disc height spaces were measured. The mean anterior disc height was 11.2 ± 4.4mm preoperatively and 11.3 ± 3.9mm at 24 months. There was no significant change in the anterior disc height space. The mean posterior disc height was 6.1 ± 2.5mm preoperatively and 7.5 ± 3.0mm at 24 months. There was a significant increase in the posterior disc height space.

M. **Safety Analysis**

Safety analyses included all patients regardless of the completeness of their follow-up data. Safety was assessed through physical examinations, x-rays, and by questioning of all patients enrolled in the study. For a summary of the safety data, please see Tables 1 and 2 in Section VIII above, Potential Adverse Effects.

From the complications previously identified in Tables 1 or 2, there are some postoperative complications that are considered to be clinically significant because they are either generally irreversible or require major surgical intervention for resolution. For this reason, the rates of these clinically significant complications are compared between the Ray TFC™ group and the literature controls. The rates shown in Table 5 below are the number patients with the clinically significant complication divided by the total number of patients in the study. Again, the complications for the Ray TFC™ group have already been identified above in Tables 1 or 2.

Table 5 - Clinically Significant Postoperative Complications

Complication	Ray TFC™ Rate	Literature Rate[1]
surgical interventions[2]	3.4%	0.5% - 11.0%
unresolved pain	3.0%	1.6% - 4.2%[3]
unresolved neurological deficit	2.5%	0% - 5.0%[4]
CSF leak	1.3%	0.5% - 3.0%
serious wound infection	0.8%	0% - 5.6%
ileus	0.4%	0.3%
death[5]	0.4%	0% - 1.1%
graft/device breakage	0.4%	1%
graft/device extrusion or migration	0%	0% - 7%
pulmonary embolus	0%	0.2% - 2.2%
gastro-intestinal (GI) bleeding	0%	0.3%
myocardial infarction	0%	0.4% - 2.9%

thrombophlebitis	0%	0%-4.8%
nephritis	0%	6.0%

[1]The literature rates were based on only the articles that reported or referenced the complication. The complication rates without a range of literature rates were reported only in one article. The literature sample sizes ranged from 13 to 750 patients.

[2]Surgical interventions includes any revisions, removals, reoperations, and supplemental fixations.

[3]It was not possible to always determine whether the pain reported in literature was unresolved or serious pain.

[4]It was not possible to always determine whether the neurological deficits reported in literature were unresolved.

[5]The death reported in the study was not related to device or procedure. It was not possible to always determine whether the deaths reported in literature were device or procedure related.

N. **Study Success / Statistical Differences**

To be considered an overall study success, the patient must have met each of the following four criteria: 1) fusion of the involved level(s); 2) improvement in pain; 3) maintenance or improvement in function; and 4) maintenance or improvement in muscle strength. The success rates at 24 months for each individual outcome parameter as well as overall success based on all four parameters are shown in Table 6. Note that the number of patients with data available differs slightly for each outcome success criteria based on the study follow-up.

Table 6 - Study Success Rates at 24 Months

Success Criteria	Rate
Fusion Rate	92% (183/200)
Pain Improvement	76% (158/209)
Function Maintenance or Improvement	96% (200/209)
Muscle Strength Maintenance or Improvement	95% (197/208)
Overall Success (met all 4 above)	64% (128/199)

Because of the many differences between the control groups and the Ray TFC™ group, the longitudinal analyses performed on the Ray TFC™ patient population was extremely

important in the assessment of the safety and effectiveness of the Ray TFC™ device. The longitudinal analyses (using Generalized Estimating Equation (GEE) model) showed that the outcomes did not worsen over time. Specifically, the rate of fusion increased with time, the amount of pain decreased with time, and the patient's ability to function increased with time.

From the longitudinal analyses of these clinical data, the following statistical differences were observed up to or at the two-year time point:

- Younger patients had lower levels of pain and higher levels of function than older patients.

- Nonsmokers had lower levels of pain and higher levels of function than smokers.

- Patients with baseline disc herniation had lower levels of pain than those without baseline disc herniation.

- Older patients with L5-S1 involvement had higher levels of pain than older patients with other levels of involvement. In younger patients, there was no significant effect on pain based on level of involvement.

- Patients who had lower baseline function scores showed lower levels of function through the study than those with higher baseline function scores.

- Older patients with L5-S1 involvement had lower levels of function than older patients with other levels of involvement. Additionally, older patients with lower baseline function scores had lower levels of function than older patients with higher baseline function scores. In younger patients, there was no significant effect on function based on level of involvement or baseline function score.

- Patients receiving worker's compensation had higher levels of pain and lower levels of function than those not receiving worker's compensation.

O. **Comparison with Literature Controls**

A total of 13 PLIF literature articles were used as controls; these are identified in Section XVII below, References. The sample sizes reported in these articles ranged from 13 to 750. As previously discussed, these literature controls were often greatly different from the Ray TFC™ population. However, clinical results and complication information were extracted for purposes of this comparison. Ray TFC™ patients at 24 months follow-up were selected for this comparison.

The fusion rate for the Ray TFC™ was 92% (183/200). The range of fusion rates reported in the PLIF literature controls was 82% to 98%. Fusion results for the Ray TFC™ were better than literature results in 7 of 13 articles and worse in 5 (1 article did

not report the fusion rate). The Ray TFC™ was not significantly worse than any literature controls.

The definition of clinical success in the PLIF literature primarily involved an assessment of pain, analgesic use, work status, and activity level. The clinical success rates reported in the PLIF literature controls based on the author's definitions of excellent and good, ranged from 24% to 91%. The clinical success rates reported in the PLIF literature controls based on the author's definitions for excellent, good, and fair, ranged from 60% to 98% Taking into consideration the same types of measurements, these literature control rates were compared to the following Ray TFC™ clinical rates: 76% (158/209) for pain and 96% (200/209) for function. It cannot be determined if the differences are due to true differences in clinical success, or due to differences in patient population, data collection, or interpretation of methods used to determine success.

The experience in this clinical investigation with the Ray TFC™ compares favorably with literature complication rates for PLIFs. Reported complications for the Ray TFC™ were within the range reported for the literature control groups. This is shown in Table 5 above in Section M, Safety Analysis.

XII. SUMMARY OF OTHER CLINICAL INVESTIGATIONS

Prior to the submission of any IDE, one of the primary investigators for the IDE study implanted prototypes of the Ray TFC™ into 10 patients under the sponsorship of another company. The patients were diagnosed as having DDD requiring posterior lumber interbody fusion (PLIF). Four of the devices were made from stainless steel and six were made from commercially pure titanium. The report of clinical and radiographic results was essentially incomplete and anecdotal. The fusion rate was reported as 91% at one year and 88% at five years. Complications included a dural tear, CSF leak, and stress cracks in the cages.

XIII. CONCLUSIONS DRAWN FROM THE STUDIES

The nonclinical (i.e., mechanical) and clinical data provide reasonable assurance of the safety and effectiveness of the Ray TFC™ for the treatment of degenerative disc disease (DDD), when used as indicated.

XIV. PANEL RECOMMENDATIONS

The Orthopedic and Rehabilitation Devices Panel met to discuss the application on May 23, 1996. The Panel recommended that the application be approved pending submission to and approval by the Center for Devices and Radiological Health (CDRH) of: a reanalysis of the study outcomes with a revised definition of patient success; modifications to the labeling; creation of a patient information document; development of post-approval studies; additional statistical analyses; and additional sterilization information regarding the end cap. The Panel agreed with FDA's recommendation to

define patient success as fusion of involved level(s); improvement in pain; maintenance or improvement in function; maintenance or improvement in muscle strength; and maintenance or improvement in neurological reflexes.

The Panel recommended that the labeling be modified to: (1) limit use to the treatment of patients with DDD where DDD is defined as back pain of discogenic origin with degeneration of the disc confirmed by historical and radiographic studies; (2) recommend a minimum of six months of non-operative treatment; (3) report the study's success rates and trends noted in the statistical analyses; (4) require that the device be packed with autograft bone; (5) limit use of the device to fusions involving one or two levels; and (6) include a warning against implantation of a single cage per involved level.

As stated above, the Panel also recommended that two post-approval studies be developed. The first post-approval study is to obtain continued follow-up for a subset of the patients from the IDE study to evaluate the long-term device performance and patient outcomes for a minimum of five years. The second post-approval study is to retrieve and analyze any Ray TFC™ device that was implanted and subsequently removed. The Panel recommended that retrieved implants be analyzed metallurgically and histologically for bone quality/quantity and potential wear debris.

XV. CDRH DECISION

CDRH agreed with each of the Panel's conditions. However, based on the major statistical analyses recommended by the Panel, FDA issued a letter to United States Surgical Corporation on June 20, 1996 advising them that the PMA lacked information needed to complete the review and to determine whether there was reasonable assurance that the device is safe and effective for its intended use. This June 20, 1996 letter included the Panel's recommended conditions of approval as well as required the following information: additional complication information; sterilization information for the instruments; revision of the labeling to incorporate all applicable changes (e.g., indications for use, clinical results, complications); modifications to the surgical technique manual; generation of a surgeon training program; and development of the post-approval studies with specific elements.

In amendments received by FDA on July 23 and August 21, 1996, United States Surgical Corporation submitted the requested information. The company reanalyzed the clinical outcomes using the revised definition of overall patient success (redefined again to be based on only fusion, pain, function, and muscle strength while capturing neurological information in the complication section), defined the patient population, performed additional statistical analyses, addressed the sterilizations issues for the end cap and instruments, revised the labeling, modified the surgical technique manual, described their surgeon training program, and developed two post-approval studies. The first post-approval study involves the collection of clinical and radiographic data for long term device performance and patient outcomes for an additional four years of follow-up (for a total of six years of postoperative data) on the IDE patient population; the goal is to

obtain six years of postoperative data on a minimum of 100 patients. The second post-approval study involves the retrieval assessment of any Ray TFC™ that is implanted and subsequently removed.

Based on the additional information submitted by United States Surgical Corporation, CDRH agreed with the Panel's recommendations that the PMA be approved subject to the conditions above. On August 29, 1996, FDA issued a letter to United States Surgical Corporation advising them that its PMA was approvable based on the conditions listed above. The one deficiency cited in the letter involved revising the surgical technique manual.

In an amendment received by FDA on September 12, 1996, United States Surgical Corporation submitted the required information which included revisions to the labeling and post-approval studies and agreed to the conditions cited in the letter dated August 29, 1996. CDRH determined that, based on the above modifications, the applicant's response was adequate.

FDA inspections completed on _____ determined the manufacturing facilities to be in compliance with the Good Manufacturing Practices (GMP) regulations.

CDRH issued an approval order on _____.

XVI. APPROVAL SPECIFICATIONS

Directions for Use: See labeling.

Hazards to Health from Use of the Device: See indications, contraindications, warnings, precautions, and adverse events in labeling.

Post-approval Requirements and Restrictions: See approval order.

XVII. REFERENCES FOR CONTROLS

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